Application No. 09/678,202 Amendment dated November 24, 2004 Reply to Office Action of May 26, 2004

## **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1. (currently amended) A method of reducing the damage done by reactive oxygen species (ROS) in an animal comprising administering to the animal an effective amount of a metal-binding peptide which does not have a metal ion bound to it, and the peptide binds a metal ion present in the animal, with the result that the damage done by the ROS is reduced, the sequence of the peptide being:

$$P_1 - P_2$$

wherein:

 $P_1$  is:

Xaa<sub>1</sub> Xaa<sub>2</sub> His or

Xaa, Xaa, His Xaa,;

 $P_2$  is  $(Xaa_4)_n$ ;

Xaa<sub>1</sub> is the N-terminal amino acid of the peptide, Xaa<sub>1</sub> has an unsubstituted  $\alpha$ -amino group, and Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>2</sub> is glycine, alanine,  $\beta$ -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>3</sub> is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa<sub>4</sub> is any amino acid; and n is 0-100;

Application No. 09/678,202 Amendment dated November 24, 2004 Reply to Office Action of May 26, 2004

or a physiologically-acceptable salt thereof.

- 2. (original) The method of Claim 1 wherein  $Xaa_1$  is aspartic acid, glutamic acid, arginine, or  $\alpha$ -hydroxymethylserine.
- 3. (original) The method of Claim 1 wherein  $Xaa_2$  is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine.
  - 4. (original) The method of Claim 1 wherein Xaa<sub>3</sub> is lysine.
- 5. (original) The method of Claim 1 wherein  $Xaa_1$  is aspartic acid, glutamic acid, arginine, or  $\alpha$ -hydroxymethylserine,  $Xaa_2$  is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine, and  $Xaa_3$  is lysine.
- 6. (original) The method of Claim 5 wherein  $Xaa_1$  is aspartic acid or glutamic acid and  $Xaa_2$  is alanine, glycine, valine, threonine, serine, or  $\alpha$ -hydroxymethylserine.
- 7. (original) The method of Claim 6 wherein  $Xaa_2$  is alanine, threonine or  $\alpha$ -hydroxymethylserine.
  - 8. (original) The method of Claim 7 wherein Xaa<sub>1</sub> is aspartic acid and Xaa<sub>2</sub> is alanine.
  - 9. (original) The method of Claim 1 wherein n is 0-10.
  - 10. (original) The method of Claims 9 wherein n is 0-5.
  - 11. (original) The method of Claim 10 wherein n is 0.
- 12. (withdrawn) The method of Claim 1 wherein P<sub>2</sub> comprises a metal-binding sequence.
- 13. (withdrawn) The method of Claim 12 wherein P<sub>2</sub> comprises one of the following sequences: (Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>3</sub> His Xaa<sub>2</sub> Xaa<sub>5</sub>,

wherein Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub> and m is 0-5.

14. (withdrawn) The method of Claim 13 wherein Xaa<sub>5</sub> is Orn or Lys.

- 15. (withdrawn) The method of Claim 1 wherein at least one of the amino acids of  $P_1$  other than  $\beta$ -alanine is a D-amino acid.
- 16. (withdrawn) The method of Claim 15 wherein Xaa<sub>1</sub> is a D-amino acid, His is a D-amino acid, or both Xaa<sub>1</sub> and His are D-amino acids..
- 17 (withdrawn) The method of Claim 16 wherein all of the amino acids of  $P_1$  other than  $\beta$ -alanine are D-amino acids.
- 18. (withdrawn) The method of Claim 15 wherein at least 50% of the amino acids of P<sub>2</sub> are D-amino acids.
- 19. (withdrawn) The method of Claim 16 wherein at least 50% of the amino acids of P<sub>2</sub> are D-amino acids.
- 20. (withdrawn) The method of Claim 17 wherein at least 50% of the amino acids of P<sub>2</sub> are D-amino acids.
- 21. (original) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because of the need to reperfuse an ischemic tissue or organ of the animal.
- 22. (original) The method of Claim 21 wherein the animal is suffering from cerebrovascular ischemia and the ischemic tissue is located in the brain of the animal.
- 23. (original) The method of Claim 21 wherein the animal is suffering from cardiovascular ischemia and the ischemic tissue is located in the heart of the animal.
- 24. (original) The method of Claim 21 wherein the peptide is administered prior to reperfusion, simultaneously with reperfusion, after reperfusion, or combinations thereof.
- 25. (withdrawn) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because of neurological trauma.
- 26. (withdrawn) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from a neurodegenerative disease.
  - 27. (canceled)

- 28. (previously presented) The method of any one of Claims 1-20 wherein the peptide is administered to an animal exhibiting symptoms of possible cerebrovascular ischemia or possible cardiovascular ischemia while the animal is being diagnosed.
- 29. (previously presented) The method of any one of Claims 1-20 wherein the peptide is administered to an animal prior to surgery, during surgery, after surgery, or combinations thereof.
- 30. (original) The method of Claim 29 wherein the surgery is open-heart surgery or surgery to transplant an organ into the animal.
- 31. (withdrawn) The method of any one of Claims 1-20 wherein the peptide is administered to an animal prior to radiation therapy, during radiation therapy, after radiation therapy, or combinations thereof.

Claims 32 - 374 (canceled)

- 375. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from ischemia.
- 376. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from ischemia of the central nervous system.
- 377. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from a stroke.
- 378. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from cardiovascular ischemia.
- 379. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from myocardial ischemia.
- 380. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from acute myocardial infarction.
- 381. (previously presented) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from angina pectoris.